Concept Clearance

Branch: ERTB

Council Period: 201805

Concept Title: The Human Health Exposure Analysis Resource

Introduction

The Children's Health Exposure Analysis Resource (CHEAR) was supported in 2015 with funds redirected from the National Children's Study to establish an infrastructure to support the analysis of environmental exposures in NIH funded studies focused on children's health. The emphasis of CHEAR is on the addition of exposure analysis in biological samples to those studies that have not previously considered environmental exposures and the expansion of studies that have assessed exposures to consider exposure on a more comprehensive scale. Ultimately, CHEAR seeks to serve as a demonstration of the potential for integrating exposome analysis in to existing children's health studies through the untargeted discovery of associations between exposures and health outcomes. The Consortium is a full-service analytical infrastructure with a Coordinating Center providing outreach and logistical support, a Network of Laboratory Hubs providing targeted, untargeted, and biological response analyses, and a Data Center providing a public access data repository and statistical and informatic analytical support.

In the first year of funding, CHEAR focused on establishing internal operating procedures, harmonizing analyses to international proficiency standards, and public outreach. In the second year of support, CHEAR began accepting applications from the NIH grantee community and supporting analyses. To date, CHEAR has approved more than 30 studies including more than 43,000 sample analyses, with the results of the first few being analyzed and shared with the clients. These studies cover a broad landscape of exposures and children's health outcomes and are likely to support the harmonization of findings across studies supported by the program.

Research Goals and Scope

The fundamental goal of the recompetition will be unchanged; to support an infrastructure that provides centralized, high quality exposure assessment across the breadth of the exposome to the grantee community. The consortium will continue to function as a full-service infrastructure of laboratories, data, and coordinating centers which will provide value both to the individual client utilizing the resource and the broader community through enhanced data sharing and resources including an overarching ontology for exposure analysis and the development and validation of new methods.

Building on the experiences in the first three years of the CHEAR Program we propose relatively few changes of the second phase of the infrastructure. The most significant of these will be a shift in the central focus from a limited scope of children's exposure and health to encompass all human health and life stages (prenatal through adulthood) and a rebranding of CHEAR to be HHEAR – the Human Health Exposure Analysis Resource. This will increase our understanding of the influence of environment on health throughout the life-course and eventually support more comprehensive assessment of the Developmental Origins of Health and Disease. This will also expand the access to this resource to a more expansive community of potential clients.

The overarching structure and focus of the components of the consortium will be essentially unchanged from the initial CHEAR infrastructure. The only significant structural change at the outset of the program is to increase the focus on the fundamental goal of exposure analysis by removing the Biological Response Indicator Resource (BRIR) component of the laboratories. The offerings of the BRIR across the network are highly divergent and has proven to be a great challenge to standardize and harmonize and in many cases are duplicative of resources otherwise available to clients through their local institutions or commercial sources.

Two additional components to the network will be solicited in future years. The first is a new laboratory type to include *analysis of environmental samples* linked to health endpoints. This includes both analysis of dust, soil, water, and air filters to provide greater insight to the sources and routes of exposure linked to health outcomes. This component will also serve as a 'clearinghouse' for evaluation and provision of personal/wearable sensors and remote sensing technologies to the client community. As with any project utilizing the HHEAR resource, the focus would be on the addition of exposure measures to an NIH funded project and require sharing of phenotypic data through the HHEAR data repository. The second new component is a secondary data analysis program to support access to and comprehensive analysis of data provided by the HHEAR Data Center.

Mechanism and Justification

There are five components to the program which will be solicited through open competitions:

- One Coordinating Center supported as a U24
- One Data Center supported as a U2C

- Two or more Biomonitoring laboratories supported as a U2C
- One or Two Environmental Monitoring laboratories
- A small grant program to support secondary data analysis (R03)

The Coordinating Center and Data Center components of HHEAR will be largely unchanged from the currently supported goals. The Coordinating Center will continue to focus on internal working and logistics as well as education, outreach, and publicity. The Data Center will also continue with the three-fold mission of serving as a public access data repository, data science framework for exposure, and statistical consulting and analysis center.

Based on the NIEHS Epidemiology Resource, NIEHS supported epidemiological studies have enrolled more than 145,000 participants who have provided at least one biological sample which could be analyzed by HHEAR. Experience of CHEAR to date indicates that the typical client will request an average of 2.5 analyses per sample and many will also request multiple time points on an individual participant. It is impossible to know the total potential number of analyses to be requested but is clear that support at an anticipated analytical capacity of an individual laboratory of approximately 15,000 samples annually will allow for a high degree of selectivity in the studies approved.

We propose that the laboratories will continue to operate as 'prepaid' full-service laboratories. Analysis of the cost model shows this to be the optimal arrangement for efficiency and quality. The cost of targeted and untargeted analysis varies based on sample matrix and analyte; this averages to approximately $150 per sample for targeted (and between $200 and $300 for untargeted) regardless of the funding model used presuming a workload that generates economies of scale. Of this fee the majority (85-90%) is 'fixed' costs of personnel, equipment, maintenance, and overhead, while the remainder is consumables. Continuing with the model of 'prepaid' full service allows for continuity of personnel and equipment and results in more stability for the resource and improved quality given that stability; while a 'fee-for service' incurs additional costs associated with changing demand for specific analyses.

NIEHS is considering the addition of two new activities which will be implemented in the later stages of the program. The first is in response to several inquiries received by the CHEAR consortium expressing interest in analysis of samples from the participants' living environment such as dust, soil, water, and air monitoring filters as an additional layer of information on the exposures influencing health outcomes. Delaying the start of this laboratory will allow an immediate focus on the transition of the biomonitoring activities, data center, and coordination from CHEAR to HHEAR while also assessing the demand and needs for the environmental monitoring component. Similarly, a small grant program to incentivize the reanalysis of public access data provided by CHEAR and HHEAR will be delayed until a critical mass of public access data is provided by the repository.

A final distinction of HHEAR from CHEAR will be the implementation of a 'Pay to Play' model with other NIH Institutes and programs. Currently, CHEAR is available to studies supported by any NIH Institute due to the fact that the money that has supported CHEAR was redirected from a trans-NIH program. In the recompetition the scope of eligible clients will be limited to those ICs and programs who contribute funds to the program. To date this includes NIEHS and the NIH Environmental Influences on Child Health Outcomes (ECHO) Program which is currently supporting the CHEAR program and has committed to continued support to provide access to CHEAR/HHEAR capabilities in support of both ECHO multi-cohort analyses and the ECHO Common Protocol through 2022. Several other NIH Institutes are considering participation including NIAID, NCI, NIA, NICHD, NIDDK, and NHLBI and may consider support for the consortium to provide access to all of their grantee community or to specific programs. Any such support will be used to fund additional laboratories or add capacity to those funded through HHEAR and to supplement the efforts of the single Data and Coordinating Centers.

To maximize the impact of HHEAR over time and enhance the stability of the resource to support programs such as ECHO; approval from NIH will be sought to fund the consortium for seven years.